COUGH AND BRONCHIAL RESPONSIVENESS IN FIREFIGHTERS AT THE WORLD TRADE CENTER SITE

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ABSTRACT

Background Workers from the Fire Department of New York City were exposed to a variety of inhaled materials during and after the collapse of the World Trade Center. We evaluated clinical features in a series of 332 firefighters in whom severe cough developed after exposure and the prevalence and severity of bronchial hyperreactivity in firefighters without severe cough classified according to the level of exposure.

Methods "World Trade Center cough" was defined as a persistent cough that developed after exposure to the site and was accompanied by respiratory symptoms severe enough to require medical leave for at least four weeks. Evaluation of exposed firefighters included completion of a standard questionnaire, spirometry, airway-responsiveness testing, and chest imaging.

Results In the first six months after September 11, 2001, World Trade Center cough occurred in 128 of 1636 firefighters with a high level of exposure (8 percent), 187 of 6958 with a moderate level of exposure (3 percent), and 17 of 1320 with a low level of exposure (1 percent). In addition, 95 percent had symptoms of dyspnea, 87 percent had gastroesophageal reflux disease, and 54 percent had nasal congestion. Of those tested before treatment of World Trade Center cough, 63 percent of firefighters (149 of 237) had a response to a bronchodilator and 24 percent (9 of 37) had bronchial hyperreactivity. Chest radiographs were unchanged from precollapse findings in 319 of the 332 with World Trade Center cough. Among the cohort without severe cough, bronchial hyperreactivity was present in 77 firefighters with a high level of exposure (23 percent) and 26 with a moderate level of exposure (8 percent).

Conclusions Intense, short-term exposure to materials generated during the collapse of the World Trade Center was associated with bronchial responsiveness and the development of cough. Clinical and physiological severity was related to the intensity of exposure. (N Engl J Med 2002;347:806-15.)

THE September 11, 2001, terrorist attack that resulted in the collapse of New York City's World Trade Center led to an intense, short-term exposure to inorganic dust, products of pyrolysis, and other respirable materials. The Fire Department of New York City (FDNY) operated a continuous rescue and recovery effort at the site involving approximately 11,000 firefighters, who were exposed to such respiratory irritants,[1] which have been implicated in the development of airflow obstruction.[2,3] We identified conditions associated with airway obstruction — namely, severe, persistent cough ("World Trade Center cough") and airway reactivity — in exposed firefighters by assessing a case series of 332 firefighters with World Trade Center cough who required extensive medical leave as well as other firefighters who had been exposed but who did not require medical leave.

METHODS

Study Subjects

The Bureau of Health Services of the FDNY designated firefighters as having a high level of exposure if they arrived at the scene during the collapse of the World Trade Center on the morning of September 11, 2001 (day 1), a moderate level of exposure if they arrived after the collapse but within the first two days; a low level of exposure if they arrived between days 3 and 7; and no exposure if they were not at the site during at least the first two weeks of the rescue operation. FDNY officers used FDNY dispatch records to classify personnel according to the level of exposure, but owing to the high rate of self-deployment to the scene, the final designation was based on a self-administered questionnaire devised by the Bureau of Health Services and, when possible, confirmatory interviews. Among 11,336 firefighters employed by the FDNY on September 11, 2001, 343 died at the World Trade Center and 10,116 of the 10,993 surviving firefighters were subsequently evaluated as part of the medical monitoring program. Figure 1 shows the exposure status of the 10,116 firefighters who were evaluated; World Trade Center cough was diagnosed in 332, and 102 of the 9784 firefighters evaluated who did not have this condition (1 percent) were tested for bronchial hyperreactivity. World Trade Center cough was defined as a persistent cough that developed in a firefighter after exposure to the site and that was accompanied by respiratory symptoms severe enough for FDNY physicians to place the worker on medical leave for at least four consecutive weeks.

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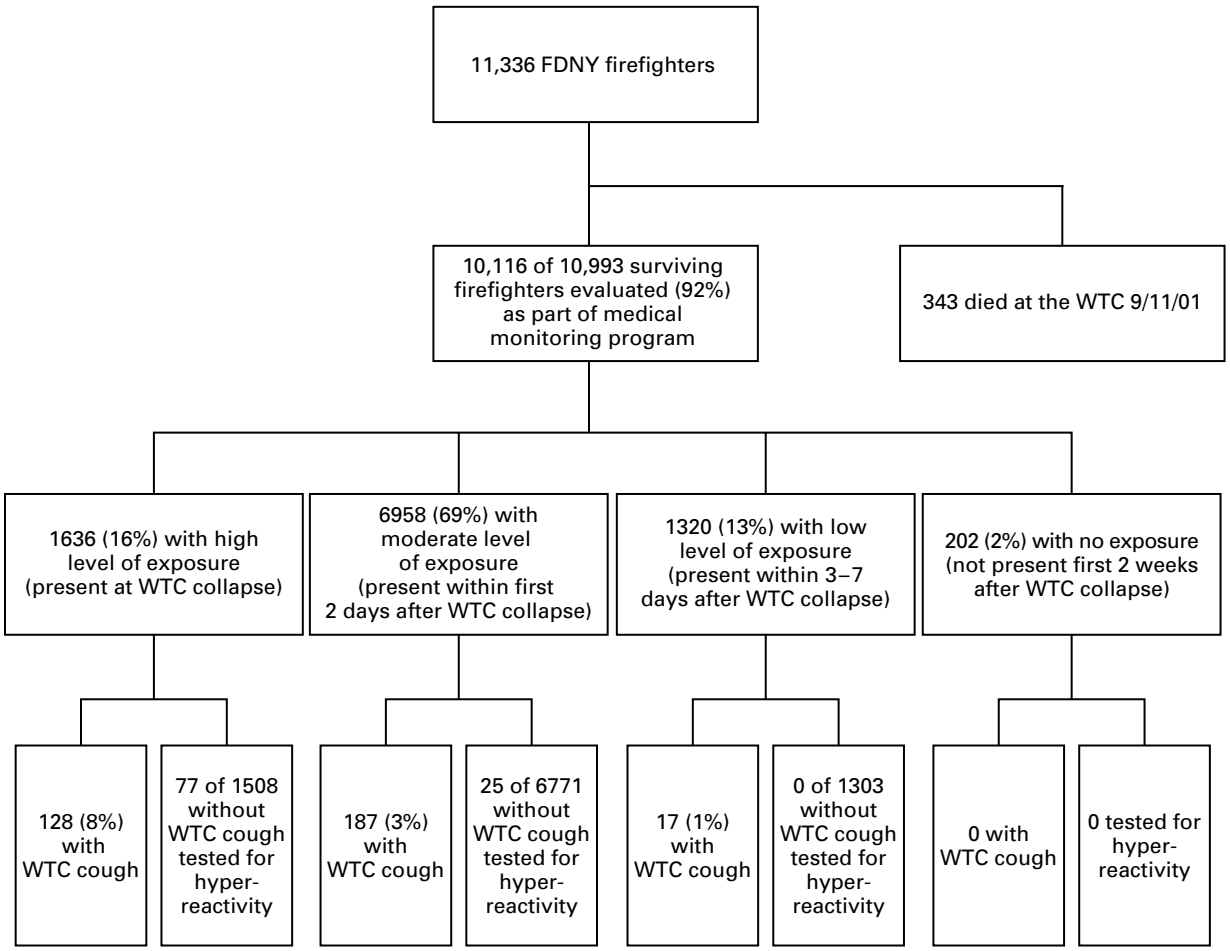

Figure 1. Number of Firefighters Employed by the Fire Department of New York City (FDNY) on September 11, 2001, and Number Who Were Subsequently Evaluated for World Trade Center (WTC) Cough and Bronchial Hyperreactivity, According to the Level of Exposure to Respiratory Irritants at the Site of the Collapse.

The study was approved by the research review board of the Montefiore Medical Center.

Bronchial Hyperreactivity in Exposed Firefighters without World Trade Center Cough

Approximately one month after the collapse of the World Trade Center (October 1 to 14, 2001), a sample of firefighters with moderate and high levels of exposure underwent a methacholine challenge to test for bronchial hyperreactivity. Among the 295 such workers who registered for the required medical evaluation during this interval, every second one was offered the opportunity to participate, regardless of the presence or absence of symptoms. All subjects remained on full duty, and the results of the challenge did not alter their duty status. All subjects gave written informed consent.

World Trade Center Cough in Exposed Firefighters

This report includes cases of World Trade Center cough identified from September 11, 2001, through March 11, 2002. Case ascertainment is complete, since all FDNY firefighters who are on medical leave must report to the Bureau of Health Services for evaluation. Firefighters with World Trade Center cough either referred themselves for an evaluation of symptoms or were identified during the mandatory medical evaluation or on the basis of worker-compensation claims of injury or illness or applications to the FDNY for disability leave or retirement.

Diagnostic and Treatment Protocol

The standardized protocol (see Supplementary Appendix 1, available with the full text of this article at http://www.nejm.org) included an evaluation involving self-administration of the questionnaire, supplemented by history taking and a physical examination by a Bureau of Health Services physician. The questionnaire included queries about the time of arrival at the World Trade Center site, days spent at the site during the first two weeks, the type of respiratory protection worn (a dust mask, N95 respirator, or dual-cartridge half-face P-100 respirator), and the frequency of respirator use (never or rarely used vs. used most of the time) during the first two weeks after the collapse. Health-related questions were included about nasal and throat symptoms (nasal drip, nasal congestion,

and sore or hoarse throat), symptoms of gastroesophageal reflux disease (defined as heartburn, regurgitation, and retrosternal chest burning), and respiratory symptoms (defined as daily cough, nearly constant cough, wheeze, shortness of breath, chest tightness, and sleep disturbance due to respiratory symptoms). To be considered related to exposure to the World Trade Center site, symptoms had to be new or definitely worse since September 11, 2001.

A chest radiograph was obtained and spirometry was performed in all 332 firefighters with World Trade Center cough, and 237 also underwent postbronchodilator spirometry. Lung volumes and carbon monoxide diffusing capacity were measured in the first 81 firefighters with World Trade Center cough, and because the results were within normal limits in these subjects, they were performed in only 27 subjects thereafter at the discretion of a physician. A methacholine challenge was performed in 196 firefighters with World Trade Center cough. Noncontrast high-resolution computed tomographic (CT) imaging of the chest was performed at the discretion of their physician in 78 firefighters with World Trade Center cough who had normal chest radiographs. All firefighters with World Trade Center cough were included in the study data base, even if they did not undergo all tests.

Cough was treated with cough suppressants (containing codeine) as needed. In addition, subjects received inhaled (pulmonary or nasal) or oral corticosteroids, decongestants, antibiotics, leukotriene modifier (montelukast), or proton-pump inhibitors, depending on whether they presented with predominantly upper-airway or lower-airway findings (see Supplementary Appendix 1). In firefighters with World Trade Center cough, an upper-airway predominance was defined by nasal congestion or drip, gastroesophageal reflux disease, or both in the presence of normal findings on chest radiography and spirometry (a forced vital capacity [FVC] or forced expiratory volume in one second [FEV_1] that was at least 80 percent of the predicted value) and the absence of treatment with an inhaled bronchodilator, an oral corticosteroid, or montelukast. A decongestant, a nasal corticosteroid, and an antibiotic were given for nasal congestion or drip, and a proton-pump inhibitor and dietary recommendations were given for gastroesophageal reflux disease. In firefighters with World Trade Center cough, a lower-airway predominance was defined by severe dyspnea, wheeze, or both in the presence of abnormal spirometric results (FVC or FEV_1 that was at least 15 percentage points lower than the value before exposure or less than 65 percent of the predicted value). Treatment included antibiotics, inhaled corticosteroids, bronchodilators, and in subjects with an inadequate therapeutic response, 10 mg of montelukast per day orally, with or without 40 mg of systemic prednisone per day (tapered over a period of one to two months).

Pulmonary Function and Airway Hyperreactivity

Before September 11, 2001, spirometry was performed every one to two years in all FDNY firefighters. After the collapse of the World Trade Center, spirometry was performed before treatment was initiated, and the results were compared with those of the most recent analysis (obtained within the preceding one to two years). Postbronchodilator spirometry was assessed 15 minutes after the inhalation of albuterol, and an increase in the FEV_1 by at least 12 percent and at least 200 ml was considered clinically significant.[4-6] Lung volumes and carbon monoxide diffusing capacity were determined with the use of helium-dilution and single-breath methods, respectively. Methacholine challenge testing was performed with the following exclusion criteria: an FEV_1 that was 65 percent of the predicted value or less, nonreproducible flow-volume loops, use of an inhaled or systemic corticosteroid within the preceding month, or current smoking (among those evaluated as part of the screening program). Increasing concentrations of aerosolized methacholine (Provocholine, Methapharm) were inhaled until the FEV_1 declined by 20 percent from the base-line value (PC_{20}) or the maximal concentration was reached (25 mg of methacholine per milliliter). Bronchial hyperreactivity was defined as a PC_{20} of 8 mg of methacholine per milliliter or less.[7-9] Bronchial responsiveness was defined as a bronchodilator response or bronchial hyperreactivity ($PC_{20} \leq 16$ mg of methacholine per milliliter). All tests met the standards and guidelines of the American Thoracic Society,[4,7] and the results were calculated on the basis of predicted values.[5,10]

Radiographic Studies

In all subjects, posteroanterior chest radiographs were obtained and compared with base-line chest radiographs obtained before September 11, 2001 (usually within the preceding one to two years). A total of 78 firefighters with World Trade Center cough underwent high-resolution CT of the chest at full inspiration and end expiration. Sections that were 1 mm thick were obtained at 10-mm intervals and evaluated for airway and parenchymal abnormalities. The images were read independently by two readers who had no knowledge of the subjects' exposure status or clinical findings; differences of opinion were settled by consensus.

Statistical Analysis

Continuous variables are expressed as means ±SD, and categorical variables are expressed as relative frequencies or percentages. Hyperreactivity was analyzed as a dichotomous variable at two cutoff points (PC_{20} of 8 mg per milliliter or less or PC_{20} of 16 mg per milliliter or less). Using analysis of variance, t-tests, or chi-square tests as appropriate, we compared the clinical characteristics among exposure groups and among subjects with World Trade Center cough according to prognostic subgroups: those with predominantly upper-airway symptoms (29 subjects) or lower-airway symptoms (95 subjects) or those with bronchial responsiveness (249 subjects). The lengths of medical leaves were compared with use of the Mann–Whitney U test. We used logistic regression to assess our outcome (resumption of firefighting duties) after adjustment for age, smoking status, and the presence or absence of airflow obstruction; results are expressed as odds ratios and 95 percent confidence intervals. A P value of less than 0.05 was considered to indicate statistical significance. All tests were two-tailed and performed with use of SPSS software.

RESULTS

Airway Hyperreactivity in Exposed Firefighters without World Trade Center Cough

Between October 1 and 14, 2001, 391 firefighters underwent medical screening examinations and 295 met the criteria for exposure, 102 of whom underwent methacholine or bronchodilator challenge. Clinical characteristics (sex, age, smoking status, and presence or absence of respiratory symptoms) did not differ significantly either between the subjects who were eligible for testing and the subjects who actually were tested or among the subjects in the two highest exposure groups (data not shown). In this cohort of 295 firefighters, the average age was 41±7 years, the mean tenure at the FDNY was 13±6 years, and 13 percent were exsmokers. All reported cough within 24 hours after exposure, and none were on medical leave. The mean FVC and FEV_1 values were within normal limits in all groups. In the group of firefighters with a moderate level of exposure, the subjects who were eligible for testing had significantly higher FVC and FEV_1 values than did subjects who were actually tested (FVC, 96 percent vs. 89 percent of the predicted value; $P=0.04$; and FEV_1, 98 percent vs.

91 percent of the predicted value; P=0.003). Among tested subjects there were no significant differences between the mean spirometric values obtained before the collapse of the World Trade Center and those obtained afterward (FEV_1, 103 percent and 95 percent of the predicted value, respectively; FVC, 98 percent and 92 percent of the predicted value). Among the four exposure groups, there were no significant differences in respirator use during the first week (fewer than 22 percent reported frequent use).

Bronchial hyperreactivity (defined by a PC_{20} of 8 mg of methacholine per milliliter or less) was present in 23 percent of firefighters with a high level of exposure (77 subjects) and 8 percent of those with a moderate level of exposure (26 subjects). Because age, smoking status, and the presence or absence of airflow obstruction may influence hyperreactivity, logistic regression was used to evaluate the association between the extent of exposure and the likelihood of hyperreactivity after adjustment for these variables. Spirometric values obtained after September 11, 2001, were used to adjust for the presence or absence of airflow obstruction. There was a significant association between the level of exposure and bronchial hyperreactivity: firefighters with a high level of exposure were more likely to have hyperreactivity than were those with a moderate level of exposure (relative risk, 21.0; 95 percent confidence interval, 1.8 to 164; P=0.01). The addition of variables related to the use of respirators had no significant effect on the results.

Table 1. Incidence of Upper- and Lower-Airway Symptoms before and after the Collapse of the World Trade Center (WTC) among Firefighters with WTC Cough, According to the Level of Exposure to Respiratory Irritants at the Site.*

Variable	High Level of Exposure (N=128)	Moderate Level of Exposure (N=187)	Low Level of Exposure (N=17)
		percent	
Cough			
Before collapse	2	2	0
After collapse	100	100	100
Upper-airway symptoms			
Nasal congestion			
Before collapse	NA	NA	NA
After collapse	51	56	47
Nasal drip			
Before collapse	NA	NA	NA
After collapse	39	42	33
Sore throat			
Before collapse	0	1	0
After collapse	82	74	80
Gastroesophageal reflux disease†			
Before collapse	4	4	18
After collapse	88	86	82
Lower-airway symptoms			
Dyspnea			
Before collapse	2	2	6
After collapse	94	96	94
Wheeze			
Before collapse	2	2	6
After collapse	57	66	77
Chest discomfort			
Before collapse	1	0	6
After collapse	86	85	82
Nocturnal symptoms‡			
Before collapse	1	1	0
After collapse	68	59	67

*To be classified as occurring after the collapse of the World Trade Center, a symptom had to be either new or more severe since September 11, 2001. Levels of exposure are defined in Figure 1. NA denotes not available.

†The symptoms of gastroesophageal reflux disease were heartburn, regurgitation, and retrosternal chest burning.

‡Nocturnal symptoms were disturbances in sleep that were due to cough, wheeze, or shortness of breath.

Firefighters with World Trade Center Cough

All 332 firefighters who met the case definition for World Trade Center cough were men (99 percent of the FDNY workforce is male); the mean age in this group was 43±7 years, and they had worked for the FDNY for a mean of 15±7 years. Twenty percent were exsmokers, and 3 percent were current smokers. All had acute cough at the time of exposure; the frequencies of other symptoms are listed in Table 1.

Sample Case Report

A healthy 45-year-old deputy chief who had never smoked arrived at the World Trade Center shortly after the second jetliner's impact. He supervised medical triage directly in front of the south tower when it collapsed. He was buried under falling debris, from which he was able to extricate himself. He reported that the air was "darker than a sealed vault and thicker than pea soup" and that he had gagging and a productive cough leading to near syncope. For two months, he had a dry cough, sore throat, nasal congestion, chest discomfort, exertional dyspnea, and nocturnal symptoms (cough, tightness of the chest, and regurgitation) — predominantly lower-airway symptoms. His cough resolved within six weeks after treatment with a cough suppressant, antibiotic, and inhaled corticosteroids.

Clinical Characteristics

Within 24 hours after exposure, all 332 firefighters with World Trade Center cough reported having a productive cough; the sputum was usually black to grayish and infiltrated with "pebbles or particles." The likelihood of World Trade Center cough was significantly related to the magnitude of exposure (P<0.01): World Trade Center cough developed in 8 percent of those with a high level of exposure (128 of 1636), in 3 percent of those with a moderate level of exposure (187 of 6958), in 1 percent of those with a low level

of exposure (17 of 1320), and in none of the firefighters with no exposure (0 of 202). Most cases occurred in firefighters with a high or moderate level of exposure (Fig. 1). Firefighters with World Trade Center cough began to seek medical attention in late September 2001. The peak incidence was in late October and early November, and by four months after the collapse of the World Trade Center, few new cases were reported (Fig. 2). The number of firefighters on medical leave was minimal in September, probably as a result of the continuing intense efforts at the World Trade Center site, but the low rate may also reflect firefighters' relatively high thresholds for reporting respiratory symptoms.

By the time of evaluation, the cough had become nonproductive in 58 percent of the firefighters. Ex-

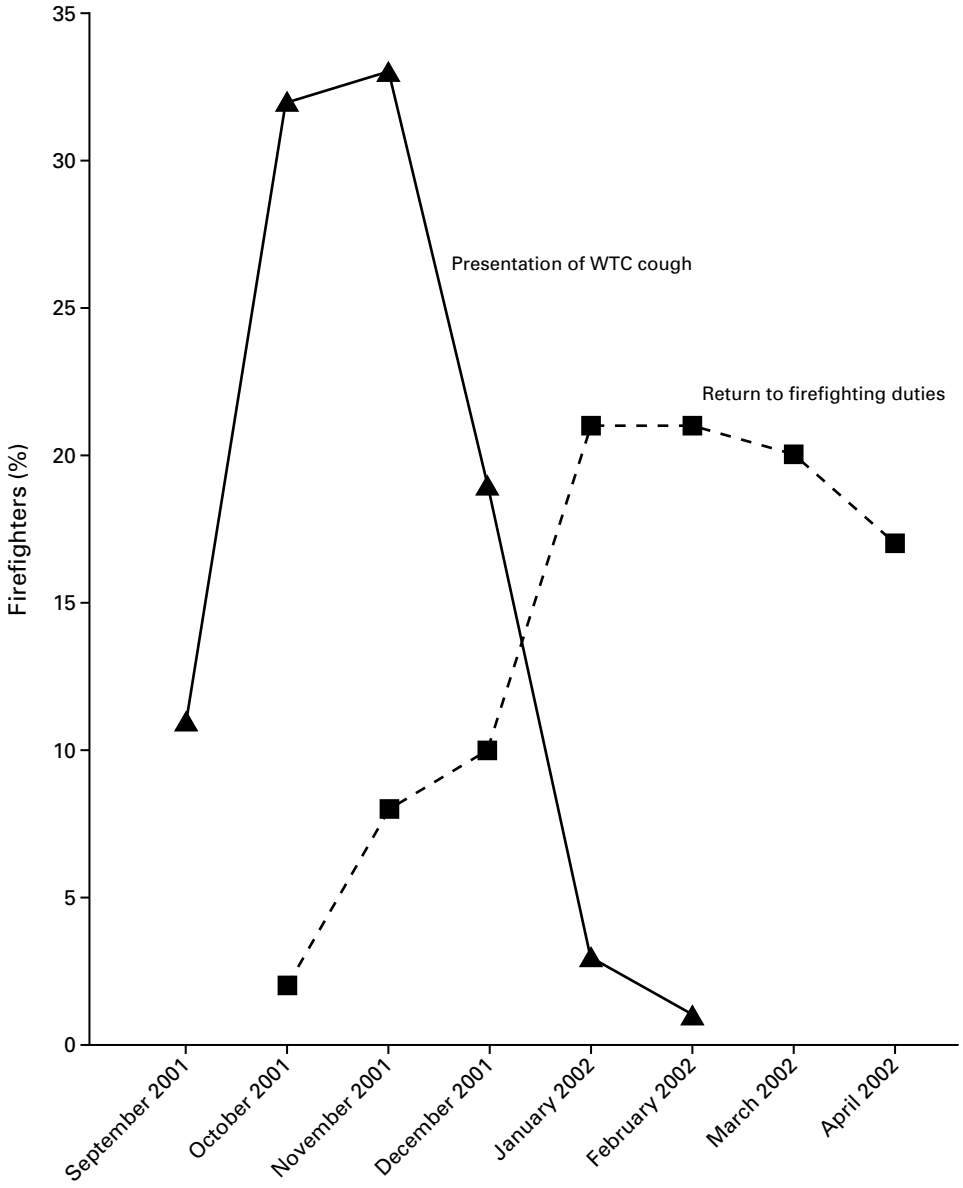

Figure 2. Clinical Course of World Trade Center (WTC) Cough.

World Trade Center cough was defined as a persistent cough that developed in the first six months after the collapse and required a medical leave from firefighting duties for at least four consecutive weeks. Return to firefighting duties (expressed as a percentage of all returning firefighters) required clearance by a Fire Department of New York City physician.

ertional dyspnea occurred in 95 percent. Upper-airway symptoms, including nasal congestion, nasal drip, and sore throat, were reported by up to 82 percent (Table 1). Overall, 87 percent had new or worsening symptoms of gastroesophageal reflux disease, which were judged by most to be severe (Table 1). The incidence of symptoms was not significantly different among the four exposure groups.

The use of respiratory protection was not associated with a significantly decreased risk of lower-airway symptoms, decreased pulmonary function, or airway hyperreactivity. However, respirators were worn rarely or not at all by 93 percent of firefighters on the day of the collapse, by 85 percent on the day after the collapse, and by 76 percent on the second through sixth days after the collapse. Even when respirators were used, the most common type was a simple paper dust mask rather than a fitted respirator certified by the National Institute of Occupational Safety and Health (self-contained breathing apparatus, N95, or dual-cartridge half-face P-100 respirator). By week 2, 65 percent of firefighters with World Trade Center cough reported frequent use of respirators, and 71 percent of those who so did used P-100 respirators.

Lung Function

Spirometric values obtained before and after the collapse of the World Trade Center are shown in Table 2. FVC and FEV_1 values were less than 65 percent of the predicted values in 1 percent of firefighters before the collapse of the World Trade Center and in 12 percent and 14 percent, respectively, after the collapse. There were significant declines in FVC ($P<0.01$), FEV_1 ($P<0.01$), and the maximal forced expiratory flow between expired volumes of 25 percent and 75 percent of vital capacity ($P<0.01$). The magnitude of the reductions in FVC and FEV_1 was nearly equal, with declines of at least 0.5 liter in 58 percent and 54 percent of firefighters, respectively. There were no significant differences in spirometric values or the magnitude of declines among the four exposure groups, but the declines tended to be least in the group with the lowest level of exposure.

Lung volumes and carbon monoxide diffusing capacity were within normal limits in 108 firefighters with World Trade Center cough who were tested. There were no significant differences in values between firefighters with abnormal findings on chest radiography and those with normal findings. Sixty-two per-

TABLE 2. SPIROMETRIC VALUES IN FIREFIGHTERS WITH WORLD TRADE CENTER (WTC) COUGH, ACCORDING TO THE LEVEL OF EXPOSURE TO RESPIRATORY IRRITANTS AT THE SITE.*

VARIABLE	BEFORE COLLAPSE OF WTC†		AFTER COLLAPSE OF WTC		AGE-ADJUSTED DECREASE
	LITERS	% OF PREDICTED	LITERS	% OF PREDICTED	LITERS
	mean ±SD (range)				
FVC					
High level of exposure	4.64±0.82	92±11 (70–120)	4.11±0.92‡	81±15 (45–108)‡	−0.62±0.78
Moderate level of exposure	4.86±0.93	95±15 (45–143)	4.25±0.80‡	83±15 (41–126)‡	−0.73±0.76
Low level of exposure	4.92±0.54	98±9 (83–107)	4.19±0.57‡	83±10 (72–105)‡	−0.40±0.59
FEV_1					
High level of exposure	3.95±0.71	95±13 (72–126)	3.43±0.75‡	82±16 (35–110)‡	−0.56±0.70
Moderate level of exposure	4.05±0.76	96±14 (46–143)	3.48±0.71‡	83±16 (39–128)‡	−0.64±0.69
Low level of exposure	4.08±0.52	99±12 (80–114)	3.46±0.47‡	84±11 (68–103)‡	−0.37±0.43
FEV_1:FVC					
High level of exposure	0.85±0.05		0.83±0.08		
Moderate level of exposure	0.84±0.06		0.82±0.08		
Low level of exposure	0.83±0.05		0.83±0.07		
$FEF_{25-75\%}$					
High level of exposure	3.96±0.93	88±17 (62–120)	3.27±1.17§	77±17 (19–107)	
Moderate level of exposure	3.88±0.94	87±17 (42–121)	3.22±0.94‡	74±15 (30–103)‡	
Low level of exposure	3.47±0.57	81±15 (66–105)	3.05±0.83	73±18 (39–95)	

*Levels of exposure are defined in Figure 1. FVC denotes forced vital capacity, FEV_1 forced expiratory volume in one second, and $FEF_{25-75\%}$ the maximal forced expiratory flow between expired volumes of 25 and 75 percent of the vital capacity.

†Values were obtained one to two years before the collapse of the World Trade Center.

‡$P<0.01$ by analysis of variance for the comparison with the value obtained before the collapse of the World Trade Center.

§$P=0.03$ by analysis of variance for the comparison with the value obtained before the collapse of the World Trade Center.

cent of the firefighters who were tested (154 of 249) had evidence of bronchial responsiveness; 53 of 332 (16 percent) had a ratio of FEV_1 to FVC of less than 0.75, 149 of 237 (63 percent) had reversible abnormalities on postbronchodilator spirometry, and 47 of 196 (24 percent) had airway hyperreactivity (defined by a PC_{20} of 16 mg of methacholine per milliliter or less) on challenge testing. Among 37 firefighters who were assessed before antiinflammatory treatment was begun, 24 percent had a PC_{20} of 8 mg of methacholine per milliliter or less and 35 percent had a PC_{20} of 16 mg per milliliter or less.

Chest Imaging

The findings on chest radiography were unchanged from base line in 319 of the 332 firefighters with World Trade Center cough (96 percent). Thirteen had lobar consolidation that resolved after antibiotic therapy. Of the 78 subjects with normal findings on chest radiography who underwent high-resolution computed tomography during inspiration and expiration (Table 3), 22 (28 percent) had no abnormalities. Air trapping was seen in 40 of the 78 (51 percent), and 12 of these patients (30 percent) had bronchial-wall thickening (Fig. 3). Seven of 38 subjects without air trapping (18 percent) had bronchial-wall thickening. Isolated parenchymal findings or parenchymal findings in combination with airway abnormalities were identified in 8 of 78 subjects (10 percent).

TABLE 3. FINDINGS ON HIGH-RESOLUTION CT OF THE CHEST IN FIREFIGHTERS WITH WORLD TRADE CENTER COUGH, ACCORDING TO THE PRESENCE OR ABSENCE OF AIR TRAPPING.*

FINDING	ALL SUBJECTS (N=78)	AIR TRAPPING (N=40)	NO AIR TRAPPING (N=38)
		no. (%)	
Bronchial-wall thickening	19	12 (30)	7 (18)
Bronchitis with inflammation of large and small airways	1	1 (2)	0
Parenchymal disease	8		
Ground-glass attenuation	5	4 (10)	1 (3)
Ground-glass attenuation and bronchial-wall thickening	1	1 (2)	0
Ground-glass attenuation and nodules	1	1 (2)	0
Ill-defined nodules and bronchial-wall thickening	1	0	1 (3)

*Images obtained during full inspiration were evaluated for bronchial-wall thickening, which was subjectively identified by comparison with known bronchial anatomy; bronchiectasis (bronchus with an internal diameter that exceeded the internal diameter of the adjacent pulmonary artery); bronchiolar impaction (clustered centrilobular nodules in a characteristic tree-in-bud pattern); mosaic attenuation; ground-glass opacities (hazy increased lung density not associated with obscured underlying vessels); nodules; consolidation; and emphysema. Images obtained during end expiration were compared with those obtained during full inspiration to identify air trapping, defined by regions of lung that did not have an increase in attenuation and a decrease in volume with expiration.

Outcomes

Within seven months after the collapse of the World Trade Center, 48 percent of the firefighters with World Trade Center cough had returned to active duty. The resumption of firefighting duties was our primary outcome, because it required medical clearance by the FDNY pulmonologist, including confirmation that pulmonary function was normal without hyperreactivity in those with prior evidence of hyperreactivity. Ninety-three percent of those with predominantly upper-airway symptoms (27 of 29) resumed firefighting duties, as compared with only 34 percent of those with predominantly lower-airway symptoms (32 of 95). Sixty-five percent of those without bronchial responsiveness (62 of 95) resumed their duties, as compared with only 20 percent of subjects with bronchial responsiveness (31 of 154). Logistic regression showed that firefighters with predominantly upper-airway symptoms were more likely to return to full duty within this six-month period than were firefighters with predominantly lower-airway symptoms (relative risk, 22.0; 95 percent confidence interval, 1.5 to 327; $P=0.03$). Firefighters without bronchial responsiveness were more likely to return to full duty than were firefighters with bronchial responsiveness (relative risk, 4.8; 95 percent confidence interval, 2.5 to 9.2; $P<0.001$).

DISCUSSION

In the first days after the collapse of the World Trade Center, firefighters and other rescue workers were exposed to enormous but unmeasured amounts of dust and other particulate materials of various sizes. The Centers for Disease Control and Prevention concluded from an evaluation of environmental data that the level of exposure to most substances (asbestos, silica, heavy metals, volatile organic compounds, and polyaromatic hydrocarbons) did not exceed limits set by the National Institute of Occupational Safety and Health or the Occupational Safety and Health Administration,[1] with concentrations of airborne and respirable particulates ranging up to 2.3 and 0.3 mg per cubic meter, respectively.[1] Fractionation of airborne dust samples revealed that 0.4 to 2 percent of particulates were respirable (that is, less than 10 μm in aerodynamic diameter; many were less than 2.5 μm) and alkaline at a pH of no more than 12 (Chen LC: personal communication). However, most samples were obtained after September 17, 2001,[1] when substantial settling of dust had already occurred. The clinical and physiological findings in patients with World Trade Center cough and the airway-responsiveness findings

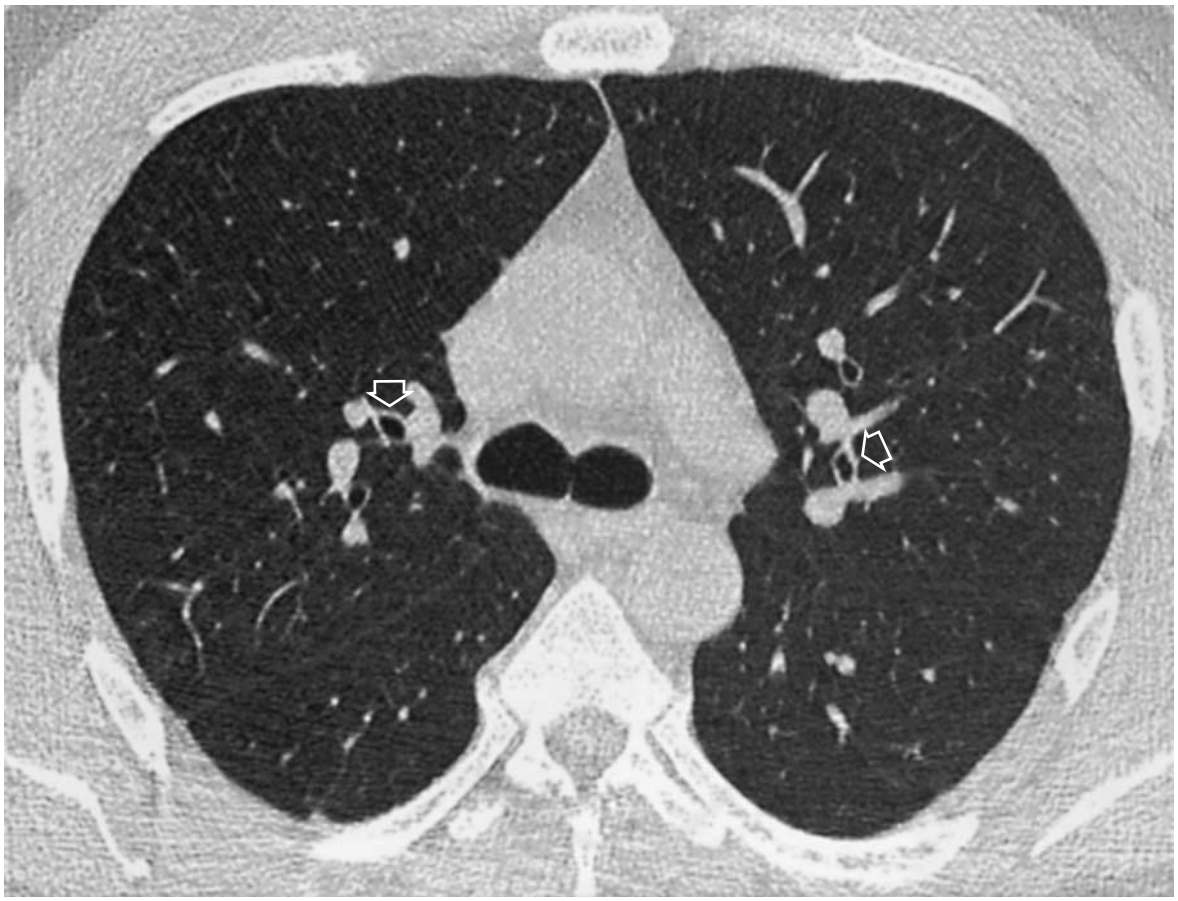

Figure 3. High-Resolution CT Images Obtained in a Firefighter with World Trade Center Cough.
A 1-mm-thick collimated section obtained at the level of the carina in a 40-year-old male firefighter shows thickening of the walls of the bronchi to the upper lobes, which is most pronounced on the left (arrows).

in the cohort of firefighters who were exposed but in whom the cough did not develop demonstrate that there was clinically significant respiratory exposure.

World Trade Center cough occurred in 3 percent of the workforce and in 8 percent of those present during the actual collapse. The majority had dyspnea, chest discomfort, gastroesophageal reflux disease, and upper-airway symptoms. Although this cohort had reductions in FVC and FEV_1 that were similar in magnitude, with no change from the FEV_1:FVC ratio determined before exposure, the findings in these subjects were predominantly attributable to airway abnormalities. Physiologically, there was a bronchodilator response and hyperreactivity; radiographically, there was air trapping and thickening of the bronchial wall without evidence of parenchymal changes.

The time of arrival at the World Trade Center site provided an effective means to categorize the intensity of exposure to respiratory irritants. It was predictive of the prevalence of airway hyperreactivity and the incidence of World Trade Center cough.

Our study is one of the few that describe the incidence of bronchial hyperreactivity after short-term exposure to respiratory irritants. Hyperreactivity occurs in miners and construction workers, but only years after long-term low-level exposure to airborne particulates.[11-13] Bronchial hyperreactivity may occur within hours after smoke inhalation.[14-16] We found hyperreactivity in about a quarter of the firefighters with high levels of exposure, whether or not they had World Trade Center cough.

Our finding of sinusitis, bronchial hyperreactivity, and bronchial responsiveness in firefighters with World Trade Center cough is important but not surprising.[17-20] An unexpected finding was that 87 percent of such firefighters reported symptoms of gastroesophageal reflux disease; such symptoms are generally reported by less than 25 percent of patients with chron-

ic cough.[1,21,22] Despite the strong associations between gastroesophageal reflux disease and chronic cough[17-20] and between gastroesophageal reflux disease and asthma,[23-25] it remains unclear whether gastroesophageal reflux disease causes either condition.[26] The causative mechanism may be repeated aspiration of minute amounts of refluxed material; vagally mediated esophageal, tracheobronchial, or laryngobronchial cough reflexes; or neurally mediated bronchial inflammation.[23,24,26] Involvement of the posterior nasopharynx is common in patients with gastroesophageal reflux disease,[27] whereas bronchial hyperreactivity may not be present.[25,26] For these reasons, we classified gastroesophageal reflux disease as an upper-airway symptom (Fig. 2).

In the firefighters who reported inhaling and swallowing dust at the site, new or worsening gastroesophageal reflux disease may have resulted from dust-induced irritation of the gastroesophageal tract. Stress related to the terrorist attack and diet are also potential causes, but neither prescription medications nor over-the-counter formulations were responsible, since the symptoms were present before treatment for gastroesophageal reflux disease was initiated.[26] Gastroesophageal reflux disease may have triggered the respiratory symptoms or may have facilitated the persistence of the airway irritation or inflammation; we believe the latter possibility is more plausible.

The firefighters with World Trade Center cough had a similar magnitude of declines in FVC and FEV_1. Similar patterns have been reported in workers exposed to inorganic particulates such as asbestos[28,29] and in brick workers,[2] whereas those exposed to toxic gas may have reduced FEV_1:FVC ratios, as was the case among victims of the industrial explosion in Bhopal, India.[30] Despite the normal FEV_1:FVC ratios in our subjects, airway obstruction was the predominant physiological abnormality. Radiographic or physiological evidence of parenchymal lung disease was uncommon, but high-resolution CT did provide evidence of air trapping. Air trapping could be due to asthma, bronchitis, emphysema, or bronchiolitis.[31,32] Bronchiolitis obliterans is a consequence of injury caused by the inhalation of a toxic substance and is characterized by either a classic pattern of obstruction or reductions in FVC and FEV_1 of a similar magnitude.[3] Since lung biopsy was not performed, we cannot exclude this diagnosis, but patients with bronchiolitis obliterans usually have no response to bronchodilators.[3]

Reactive airways dysfunction syndrome occurs after a brief, intense exposure to dust, fumes, or vapors in patients with no prior history of respiratory disease.[33-35] It is characterized by persistent symptoms of airway inflammation (cough, wheeze, and dyspnea) and bronchial hyperreactivity. In our study, the absence of respiratory symptoms or disease before September 11, 2001, was confirmed by a review of medical records. In patients with reactive airways dysfunction syndrome, respiratory symptoms and hyperreactivity persist for at least six months.[33-35] Our empirical therapy was directed at reducing inflammation through the use of nasal or inhaled corticosteroids and proton-pump inhibitors. Although this treatment was not formally tested, the circumstances did not allow us time to devise a formal treatment trial. Whether symptoms and hyperreactivity in firefighters who worked at the World Trade Center site will prove persistent, resulting in reactive airways dysfunction syndrome or airway remodeling, requires long-term study.[36,37]

Will airway hyperreactivity, obstruction, or World Trade Center cough occur in other workers and residents exposed to the byproducts of the collapse of the World Trade Center? Despite anecdotal reports of similar findings in the population at risk, our findings may overestimate the risk of this disease, because overall, FDNY firefighters most likely had the highest level of exposure. Support for this conclusion is provided by the finding that airway hyperreactivity and World Trade Center cough were more common in the firefighters with a high level of exposure. Alternatively, our findings may underestimate the risk of this disease in the population at risk, because of the healthy-worker effect. Respiratory disease (including asthma) is a medical exclusion criterion for the job of an FDNY firefighter, and frequent medical monitoring identifies firefighters with respiratory impairment and thus prevents them from performing fire-suppression duties.

The rescue and recovery efforts of firefighters at the World Trade Center site resulted in the exposure of a large cohort of workers to respirable particles and vapors. Our findings indicate that the risk of airway hyperreactivity and World Trade Center cough was associated with the intensity of exposure. During the first six months after September 11, 2001, 3 to 8 percent of firefighters with moderate to high levels of exposure had cough severe enough to require medical leave; these workers also had clinical and physiological changes consistent with the presence of upper- or lower-airway dysfunction (or both). Even firefighters without severe cough had physiological abnormalities: airway hyperreactivity was present in 8 percent of those with a moderate level of exposure and 23 percent of those with a high level of exposure. Therefore, participants in rescue and recovery work in such settings need to be aware of the health risks involved.

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